REMARKS/ARGUMENTS

In response to the final rejection of August 6, 2004, Applicants submitted an amendment under 37 C.F.R. §1.116 and a Notice of Appeal on February 7, 2004. As reported in the Advisory Action dated March 3, 2005, the amendment under 37 C.F.R. §1.116 was not entered by the Examiner. An amendment and a Request for Continued Examination were filed on March 24, 2005. In response to the Notice of Non-Compliant Amendment mailed on April 6, 2005, Applicants submit this revised amendment. Applicants herein traverse and respectfully request reconsideration of the rejection of the claims in view of the following remarks.

Claims 34-42 are pending in the application. Claims 34-42 have been rejected. Claim 34 has been amended. Support for the amendment to Claim 34 is found in the specification on Page 2, the second full paragraph from the bottom of the page. No new matter has been added. Entry of the foregoing amendment is respectfully requested.

Claims 34-42 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,048,727 (Vlasich) in view of U.S. Patent 3,709,365 (Czaplinski et al.) In particular, the Examiner states on pages 2-3:

> "Vlasich discloses a pharmaceutical package as seen in figure 1, which comprises a closed polypropylene bottle/barrel (12) in which is disposed a solution (15), the solution comprises a pharmaceutical product (col. 2, ll. 57-64), wherein the solution does not fill the bottle completely and some air is disposed in the bottle (col. 3, ll. 34-39). Vlasich lacks after autoclaving the package at at least 121°C and for at least 20 minutes, suffers no deformation, does not shrink, and does not explode and where the package retains a sufficiently high squeezability to dispense the solution. Czaplinski et al. teach the use of autoclaving a polypropylene material at about 115 -125°C. from 20-30 minutes (col. 2, ll. 49-58).
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> It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Vlasich's package by autoclaving the package, as taught by Czaplinski et al. in (col. 2, ll. 49-58) in order to treat a material that can withstand autoclaving at a temperature 121°C for at least 20 minutes."

Applicants respectfully disagree with the Examiner's conclusion and assert that the combined cited references do not make obvious the claimed subject matter as defined in amended independent Claim 34.

At the outset, it is noted that the Examiner bears the initial burden of proving a *prima facie* case of obviousness. This burden can be met by showing some objective teaching in the prior art or that knowledge that is available to one of ordinary skill in the art would motivate that individual to combine the relevant teachings of the references. In re Fritch, 972 F.2d 1260,

1265, 23 U.S.P.Q. 2d 1780, 1783 (Fed. Cir. 1992) [citing In re Piasecki, 745 F.2d 1468, 1471-72, 223 U.S.P.Q. 785, 787-88 (Fed. Cir. 1984)]. The Applicant can rebut the Examiner's *prima facie* case of obviousness by showing it was improperly made out, or by providing objective evidence which supports a conclusion of nonobviousness. *Id.* at 1265 citing In re Heldt, 433 F.2d 808, 811, 167 U.S.P.Q. 676, 678 (CCPA 1970).

With particular relevance to the present application, MPEP §2141 (Basic Considerations Which Apply to Obviousness Rejections, a copy of which is attached hereto) states in part:

> "When applying 35 U.S.C. §103, the following tenets of patent law must be adhered to:
>
> (A) The claimed invention must be considered as a whole;
>
> (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
>
> (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention...."

As demonstrated below, a *prima facie* case of obviousness has not been established. Before discussing the reasons for Applicants' conclusion, a brief summary of the presently claimed pharmaceutical package is set forth below.

The presently claimed pharmaceutical package as defined in amended independent Claim 34 comprises a closed polypropylene bottle in which is disposed a solution or gel comprising a pharmaceutical product. The solution or gel does not fill the bottle completely and some air is disposed in the bottle. The package upon autoclaving at at least 121°C for at least 20 minutes suffers no deformation, does not shrink or explode and retains a sufficiently high squeezability to dispense one drop at a time the solution or gel.

Reasons That a *Prima Facie* Case of Obviousness Has Not Been Established

1. Vlasich, when considered as a whole, fails to teach or suggest the presently claimed pharmaceutical package.

   In considering the presently claimed pharmaceutical package and the teachings of Vlasich, the Examiner's attention is directed to MPEP §2141.02 (a copy of which is attached hereto) which indicates, *inter alia*, that when ascertaining the differences between the prior art and the claims at issue, not only must the claimed invention be considered as a whole, but also the prior art reference must be considered in its entirety, i.e., as a whole,...

In the present case, the Examiner has not considered the teachings pertaining to Vlasich dispenser in its entirety as is evidenced first by the Examiner's characterization of the Vlasich dispenser as being:

> "a closed polypropylene bottle/barrel (12) in which is disposed a solution (15), the solution comprises a pharmaceutical product (col. 2, ll. 57-64), wherein the solution does not fill the bottle completely and some air is disposed in the bottle (col. 3, ll. 34-39)."

When considering the teachings of Vlasich in its entirety, the dispenser described in Vlasich is not a closed polypropylene bottle which contains both a pharmaceutical solution and some air as is asserted by the Examiner. Instead, the single dose dispenser of Vlasich (see column 2, lines 16-32 and column 3, lines 34-67) is made up of two different chambers:

- a flexible chamber containing a gas propellant such as air; and
- a rigid chamber containing a product.

The complete structure of the dispenser and its operation are shown in Figure 1 and described in column 2, lines 16-56 and column 3, lines 34-68 to column 4, lines 1-45. As set forth in Vlasich, a compressible container (12) (the flexible chamber) is filled with a gas propellant (13) such as air, and a product dispensing storage tube (14) (the rigid chamber) is filled with a predetermined dose of a composition (15) to be dispensed. The tube (14) includes a discharge opening (19) and is connected to the compressible container (12). By compressing the container (12) the air contained therein is forced to flow into the tube (14) to displace the composition (15) from the tube through the discharge opening (19). The wall (20) of the container (12) is made of a material having sufficient flexibility such as polyethylene, polypropylene, polyvinyl chloride, copolymers and the like, to permit it to bow inwardly upon application of finger pressure. The tube side wall (24) is of sufficient rigidity to resist the tendency to blow upon application of finger pressure. The composition (15) is thus prevented from being inadvertently squeezed into the container (12) filled with air.

In contrast to the two-chamber dispenser of Vlasich wherein the air and composition are in two different chambers and the two different chambers are made of different materials, the presently claimed pharmaceutical package comprises a closed bottle, i.e., one chamber, made of polypropylene, wherein the one chamber, the bottle, has disposed therein both a solution or gel comprising a pharmaceutical product and air.

Other statements made by the Examiner with respect to the Vlasich dispenser also demonstrate that the Examiner has not considered the entire teachings of Vlasich. Specifically, the Examiner at Page 2 of the final action states:

> "Vlasich lacks after autoclaving the package at at least 121°C and for at least 20 minutes, suffers no deformation, does not shrink, and does not explode and where the package retains a sufficiently high squeezability to dispense the solution."

Vlasich, however, makes clear in Figure 2, the Brief Description of the Drawings for Figure 2, and column 3, lines 5-11, that once the wall (20) of the container (12) is compressed all the air in the container is displaced and the container is in a collapsed state to dispense the entire unit dose of the product contained in the tube (14).

Indeed, the teachings of Vlasich point toward the fact that once the container (12) of the dispenser is compressed and the air flows out, the container and tube components of the dispenser remain in a collapsed state since all the air is pushed out into the tube (14) component of the dispenser. Accordingly, in contrast to the Examiner's assertion that the Vlasich dispenser suffers no deformation and retains sufficient squeezability, the two-chamber Vlasich dispenser upon discharging an entire dose of product is in a collapsed state and thus is deformed and does not retain sufficient squeezability.

As acknowledged by the Examiner there is no teaching or specific suggestion in Vlasich of autoclaving the dispenser containing the composition at at least 121°C. Indeed, Vlasich is merely concerned about the problem of dispensing an entire predetermined dosage in one discharge. Vlasich has no concern whatsoever and is completely silent regarding the problem of retaining sufficient squeezability of a pharmaceutical package upon autoclaving so that the solution or gel in the bottle can be dispensed repeatedly one drop at a time. Indeed, there is no need for the single unit dosage dispenser of Vlasich to retain sufficient squeezability as is evidenced by the purpose of such a dispenser, to discharge an entire unit dosage at one time, and the collapsed state of the dispenser upon discharging an entire dosage.

Moreover, the Vlasich dispenser is utilized one time to dispense an entire unit dosage. In contrast, the presently claimed pharmaceutical package is utilized repeatedly to dispense one drop at a time the solution or gel comprising the pharmaceutical product.

Since Vlasich when considered in its entirety, describes a dispenser possessing a completely different structure, operation and purpose from the presently claimed pharmaceutical package, it can be fairly stated that Vlasich fails to teach or specifically suggest the presently claimed pharmaceutical package as set forth in amended Claim 34.

Further, even assuming arguendo the Examiner were to assert that it would be obvious to modify the Vlasich dispenser to arrive at the presently claimed pharmaceutical package, it is asserted that such modifications would not be obvious. The Federal Court on the issue of obvious 'modifications' has instructed that:

> "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification."
>
> *Id.* at Page 1226 [citing In re Gordon, 733 F.2d at 902, 221 U.S.P.Q. at 1127]

In the present case as stated above, there is no teaching or specific suggestion to modify the structure of the single dose, two-chamber dispenser described in Vlasich to a multi-dose pharmaceutical package comprising a one-chamber polypropylene bottle which has retained a sufficiently high squeezability upon autoclavation to dispense one drop at a time the solution or gel comprising the pharmaceutical product as set forth in amended Claim 34. Further, as stated above, there is no teaching or suggestion in Vlasich to autoclave the dispenser nor is there a concern to solve the problem of autoclaving a pharmaceutical package so that it still retains a sufficient squeezability to dispense one drop at a time a solution or gel containing the product. Accordingly, Vlasich fails to suggest the desirability of such a modification.

Indeed, if the Vlasich dispenser were modified to the presently claimed pharmaceutical package comprising a polypropylene bottle suffering no deformation and retaining a sufficiently high squeezability, the modified dispenser would arguably be rendered unsatisfactory for its intended purpose, i.e., to dispense an entire dosage in a single discharge. With regard to modifying the prior art invention to arrive at the claimed invention, the Federal Court has held that if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984).

2) Vlasich teaches away from the presently claimed pharmaceutical package by teaching a two-chamber dispenser for dispensing at one time a single dose of a pharmaceutical preparation.

It is well settled that a determination of obviousness not only requires that the claimed invention be read as a whole, but also that the prior art reference be read as a whole and that:

> "consideration must be given where the references diverge and teach away from the claimed invention."
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> Akzo N.V. v. United States Intl Trade Commission, 808 F.2d 1471, 1481, 1 U.S.P.Q. 2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987).

The Federal Court has instructed that a prior art reference "teaches away" when one of ordinary skill, upon reading the reference, would be discouraged from following the path

set out in the prior art reference, or alternatively, would be led in a direction divergent from the path that was taken by the applicant. In re Gurley, 31 U.S.P.Q. 2d 1131 (Fed. Cir. 1994).

In view of the above instruction, it can fairly be said that Vlasich, in teaching a two-chamber dispenser that collapses upon discharge of an entire dosage at one time, i.e., a dispenser that suffers deformation and loss of sufficient squeezability, specifically teaches away from the presently claimed pharmaceutical package comprised of a closed polypropylene bottle which suffers no deformation and which retains sufficiently high squeezability for repeated use so that it can easily dispense one drop at a time the solution or gel comprising the pharmaceutical product. Accordingly, one skilled in the art armed with the teaching of Vlasich would be led in a direction divergent from the path that was taken by the Applicants, that is, one skilled in the art would not have chosen to construct a pharmaceutical package that retains sufficient squeezability to repeatedly dispense one drop at a time a solution or gel containing a pharmaceutical product.

3) The teachings of Czaplinski et al. when considered as a whole and combined with Vlasich fail to teach or specifically suggest the presently claimed pharmaceutical package, and thus fail to suggest the desirability of and thus the obviousness of combining Vlasich with Czaplinski et al.

Czaplinski et al. describe a radioactive generator system having a sterile, sealed disposable closure therein. As shown and described in Figure 1 and column 2, lines 3-62 of Czaplinski et al., the generator system (4) is connected to an elution bottle (12) containing an elution solution (10) via a hypodermic needle. The details of the generator system (4) are more fully set out in U.S. Patent 3,369,121 (Bruno et al., a copy of which is attached) which is referenced in Czaplinski et al. (see column 2, lines 9-11). As described in Bruno et al., the generator system houses a column which has bound to it radioactive material (see columns 2 and 3). As further described in Bruno et al. (see column 3, lines 62-75), the column, prior to its insertion in the generator system, is filled with a radioactive solution. Most of the radioactive material is absorbed onto the column and the excess radioactive material and water pass through the column and are removed. The column is then washed with acid and saline to remove any non-absorbed radioactivity and the column is sterilized, as by autoclaving. Following autoclaving, the sterilized column containing the bound radioactive material is inserted into the body of the generator.

As further described in Czaplinski et al. (see column 2, lines 3-62), the eluting solution contained in the elution bottle which is hooked up to the generator system flows through the sterilized column of the generator system and the eluate containing the radioactive

material is removed via a hypodermic needle from the bottom of the generator system and allowed to pass through conduit (22) into sterile closure (30) and then through conduit (24) into vial (20).

The sterile closure (30) comprises *inter alia*, a housing (42) wherein one end is closed by a pierceable membrane and the opposite end remains open, a membrane filter placed between the membrane and the open end, and a seal around the closed end of the housing (42) to retain the membrane in position. The purpose of the sterile closure (30) is to ensure sterility at the site of delivery of the radioactive material and reduce contamination of the generator system (see Czaplinski et al., column 1, lines 41-50).

While Czaplinski et al. (see column 2, lines 49-55) indicate that the housing material (42) can be made of a plastic, e.g., polypropylene or metal material which withstands autoclaving, e.g., about 115-125°C, it is apparent from reading Czaplinski et al., that the sterile closure (30) comprising *inter alia* the housing material (42) made of plastic or metal is sterilized prior to being connected to conduits (22) and (24) to ensure sterility at the site of delivery of the radioactive material. Importantly, Czaplinski makes clear that the radioactive material eluting from the column has already been sterilized prior to its elution from the column and is not sterilized at 115-125°C when it passes through the housing material (42) of the sterile closure (30). Thus, the radioactive material eluted from the column is not contained in the closure (30) when the closure (30) was previously sterilized. Accordingly, Czaplinski et al. fails to teach or specifically suggest autoclaving a pharmaceutical package comprising a closed polypropylene bottle which had disposed a solution or gel comprising a pharmaceutical product and air. Czaplinski et al., also fails to teach or specifically suggest that such a pharmaceutical package suffers no deformation and retains a sufficiently high squeezability to dispense one drop at a time the solution or gel. As stated above, Czaplinski et al. is merely concerned with the problem of ensuring sterility at the site of delivery of the radioactive material and to reduce contamination of the generator system. Accordingly, Czaplinski et al., as a whole, does not teach or suggest the presently claimed pharmaceutical package.

In sum, Vlasich, as a whole, teaches a two-chamber dispenser made of a flexible container containing only air and a rigid tube containing the pharmaceutical composition, which dispenser upon discharging the entire dosage at one time collapses. Vlasich is deficient *inter alia* in teaching or suggesting autoclavation of such a dispenser, and that the dispenser when autoclaved suffers no deformation and retains a sufficiently high squeezability to dispense one drop at a time the pharmaceutical composition. In addition, Vlasich, teaches away from the presently claimed pharmaceutical package, by teaching a two-chamber dispenser that discharges at one time an entire dosage, and that following discharge of the dosage from the dispenser, the dispenser is in a collapsed

state and thus suffers deformation and loses a sufficiently high squeezability. Further, if the Vlasich dispenser was modified to the presently claimed pharmaceutical package, the modification would arguably render the dispenser inoperable for its intended purpose, i.e., to discharge an entire unit dosage at one time.

Czaplinski et al., as a whole, while describing a radioactive generator system, which system *inter alia* includes a housing material made of plastic, the housing material is actually autoclaved prior to placement between conduits (22) and (24) of the generator system, and thus the radioactive solution is not contained in the housing material upon autoclavation. Accordingly, Czaplinski et al. is deficient in teaching or suggesting the elements missing from Vlasich, i.e., a closed polypropylene bottle which is disposed a solution or gel and some air, which upon autoclaving suffers no deformation and retains a sufficiently high squeezability to dispense one drop at a time the solution or gel.

Accordingly, it is difficult to see how Vlasich and Czaplinski et al. when viewed as a whole suggest the desirability of and thus the obviousness of combining Vlasich and Czaplinski et al. to arrive at the presently claimed invention as defined in amended Claim 34.

4) The §103 rejection is based on hindsight reconstruction.

It is respectfully submitted that the Examiner is relying upon hindsight to arrive at the determination of obviousness by picking and choosing separate components of the prior art references and using them to piece together the claimed subject matter without evaluating the references as a whole. The Federal Circuit has held that:

> "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination....The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.
>
> It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.
>
> In re Fritch, 23 U.S.P.Q. 1781, 1783, 1784 (Fed. Cir. 1992).

Indeed, the Federal Circuit has repeatedly cautioned against using hindsight by using the Applicants' disclosure as a blueprint to reconstruct the claimed subject matter out of isolated teachings from the prior art. See also Grain Processing Corp. V. American Maize-Products Co., 840 F.2d 902, 5 U.S.P.Q. 2d 1788 (Fed. Cir. 1988).

Since as discussed above, 1) Vlasich fails to teach or suggest a pharmaceutical package comprising a closed polypropylene bottle which is disposed both a solution or gel and air, wherein the bottle upon autoclavation suffers no deformation and retains a sufficiently high squeezability to dispense one drop at a time a solution or gel; 2) Vlasich teaches away from a pharmaceutical package dispensing one drop at a time a solution or gel and wherein such package suffers no deformation and retains sufficient squeezability; and 3) Czaplinski et al. fails to teach the elements that are deficient in Vlasich, it is clear that the Examiner has used hindsight to pick and choose among the isolated disclosures of the prior art to deprecate the present claims.

Accordingly, Vlasich and Czaplinski et al., each taken alone or combined, do not make obvious the pharmaceutical package defined in amended independent Claim 34.

In view of the above, withdrawal of the rejection of Claims 34-42 under 35 U.S.C. §103(a) is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,

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